ABSTRACT

CHEMISTRY

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ROUTES TO HIGHLY SUBSTITUTED FULVENES AND APPLICATIONS TO ORGANOMETALLIC SYNTHESIS

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Thesis dated May 1997

The goal of the research presented was to develop a high yielding method for the preparation of a tetrasubstituted fulvene and to prepare a ferrocene complex incorporating a new tetrasubstituted cyclopentadienyl ligand prepared from the fulvene. By modifying the procedure of Conia, the preparation of 3,4-dimethylcyclopent-2-enone was attempted. 3,4-dimethylcyclopent-2-enone was treated with MeLi and $[(Ph)_3P{=}CH(Ph)_2)]$ in order to synthesize diphenylmethylene-2,3-dimethylcyclopent-2-ene. The synthesis was not successful after several different modifications. Diphenylmethylene-2,3-dimethylcyclopent-2-ene was to be treated with bromine, followed by triethylamine to give 3,4-dimethyl-6,6-diphenyl fulvene.

ROUTES TO HIGHLY SUBSTITUTED FULVENES AND APPLICATIONS TO ORGANOMETALLIC SYNTHESIS

A THESIS

SUBMITTED TO THE FACULTY OF CLARK ATLANTA UNIVERSITY

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR

THE DEGREE OF MASTER OF SCIENCE

BY

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ACKNOWLEDGMENTS

I would first like to thank the Almighty God for seeing me through this trying time. Without Him, I would never have made it through this ordeal. I would also like to thank my loving parents, Dr. Archie and Mrs. Linda Wilson, who helped me to see that things could have been worse. They also helped me to see that this experience was just preparing me for the "Real World". I also thank Eric Brittain, my fiance, whom I love very much, for his undying support and love throughout this and everything. I also thank my sisters, Sophia, Arciae, and Joycelyn, for their caring. Last but not least I thank Dr. Khan for helping me to cross this final hurdle.

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LIST OF ABBREVIATIONS

THF	tetrahydrofuran
NMR	nuclear magnetic resonance
s	singlet
m	multiplet
d	doublet
t	triplet
q	quartet
Me	CH_3
Ph	$-C_6H_5$
n-Bu	$-CH_2CH_2CH_2CH_3$
CpH	cyclopentadiene
min	minute
h	hour

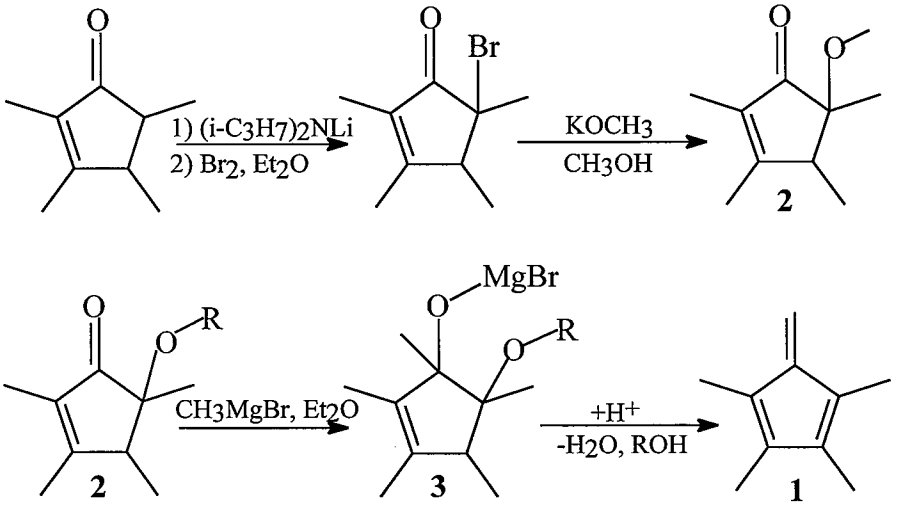
CHAPTER 1

HISTORICAL

Fulvenes are a class of compounds which have proven useful in natural product and metallocene synthesis.[1] There have been very few studies reported in the literature about the synthesis of highly substituted fulvenes, the preparation of highly substituted cyclopentadienes and subsequently, their use in organometallic synthesis.

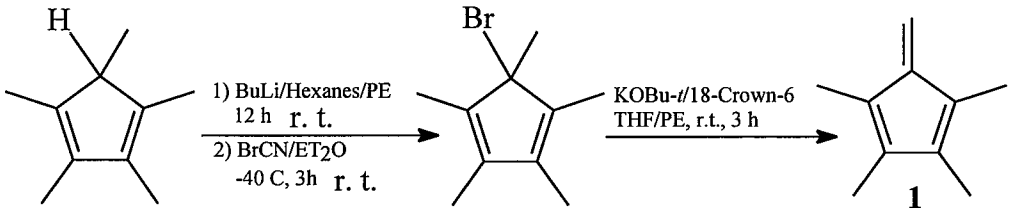
Synthesis of Highly Substituted Fulvenes

PandO and Mintz, have reported the synthesis of **1** in 74% overall yield, by the addition of methyl magnesium bromide to **2** in ether to give **3**, followed by acid catalyzed dehydration and elimination of methanol.[2]

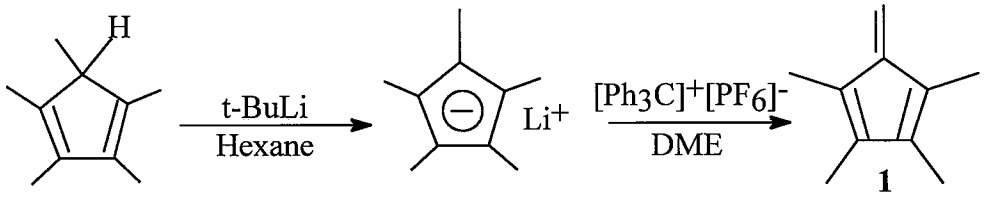


3 was obtained by the bromination of 2,3,4,5-tetramethylcyclopent-2-enone enolate and then solvolysis with $KOCH_3/CH_3OH$.

Jutzi et al., have also reported the synthesis of 1,2,3,4-tetramethyl fulvene from 5-bromo-1,2,3,4,5-pentamethylcyclopenta-1,3-diene, which is available from 1,2,3,4,5-pentamethylcyclopenta-1,3-diene in good yield. 5-bromo-1,2,3,4,5-pentamethylcyclopenta-1,3-diene reacts with potassium *tert*-butoxide in the presence of catalytic amounts of 18-crown-6 under to give **1** in high yields.[3]

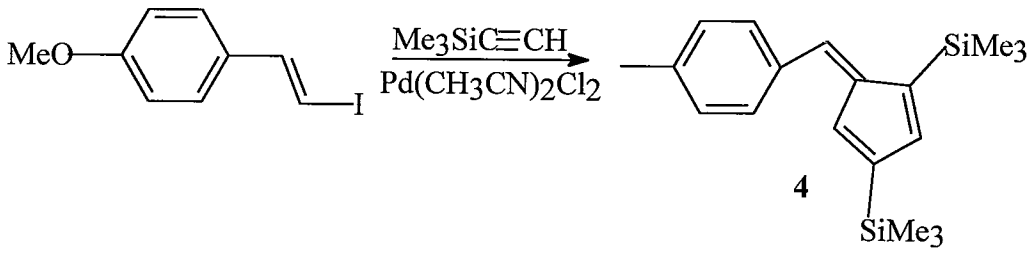


Hashimoto et al., have reported the synthesis of 1,2,3,4-tetramethyl fulvene by hydride abstraction from (pentamethylcyclopentadienyl)lithium by the addition of $[Ph_3\text{-}C]^+[PF_6]^-$ in a mixture of hexane and DME.[4] Pure **1** was isolated as an orange oil in 65% yield by column chromatography.



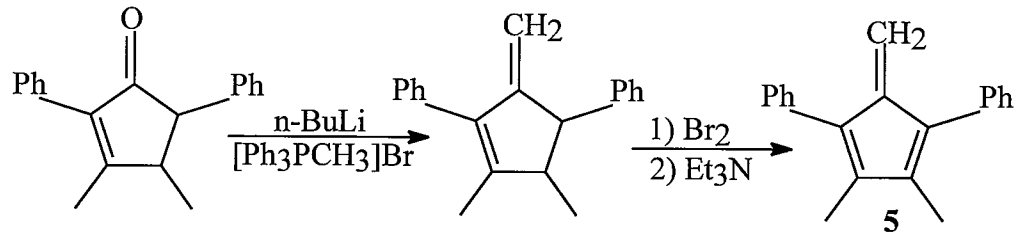
Lee et al., have reported a new synthesis for tri-substituted fulvenes. Fulvene **4** was obtained by exposure of 2-(4-methoxyphenyl)-1-iodoethene to

trimethyl silylacetylene and 5 mol% of $Pd(CH_3CN)_2Cl_2$ in (*N,N*)-dimethyl formamide.[5]



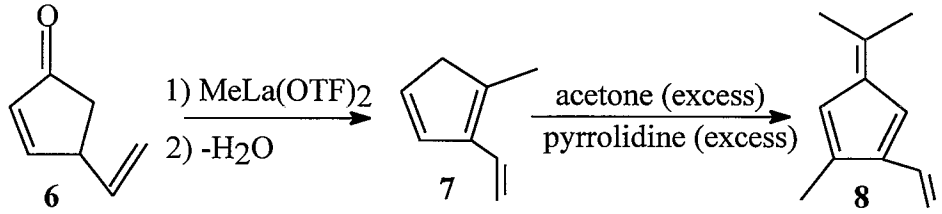
4

Donovalova et al., have reported the synthesis of 2,3-dimethyl-1,4-diphenylfulvene, **5**. Addition of $Ph_3P{=}CH_2$ to 3,4-dimethyl-2,5-diphenylcyclopent-2-enone gave the corresponding diene. The diene was then brominated and dehydrobrominated to give 2,3-dimethyl-1,4-diphenylfulvene, **5**.[6]



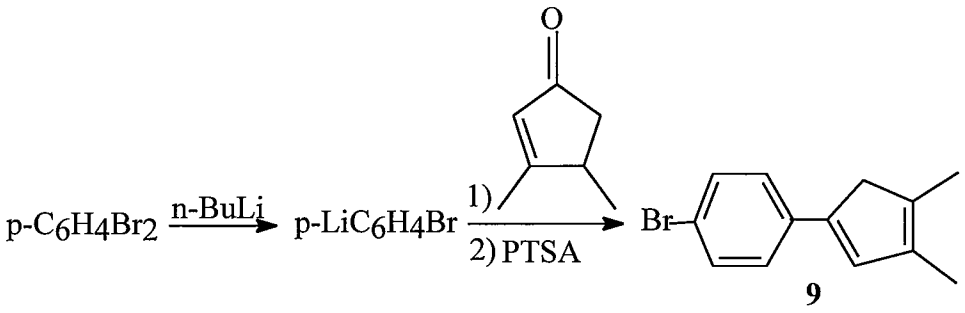
5

Collins et al, have reported the synthesis of **8**.[7] The addition of 2 equivalents of $MeLa(OTF)_2$ to **6**, followed by dehydration gave **7** in 75% yield. The subsequent addition of excessive amounts of acetone and pyrrolidine, plus MeOH to **7** gave **8** in 75% yield.[7]

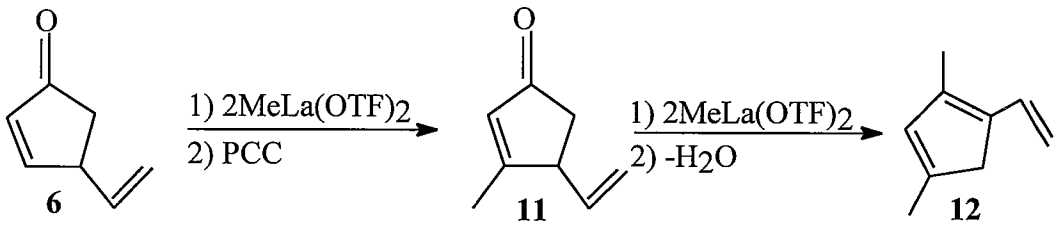


Synthesis of Highly Substituted Cyclopentadienes and Highly Substituted Cyclopentadienyl Ligands

Bunel et al., have reported the synthesis 1-(*p*-bromophenyl)-3,4-dimethylcyclopentadiene, **9**, by the addition of n-BuLi to $C_6H_4Br_2$ followed by the addition of 3,4-dimethylcyclopent-2-enone, and then dehydration by the addition of *p*-toluenesulfonic acid monohydrate in 66% yield.[8]

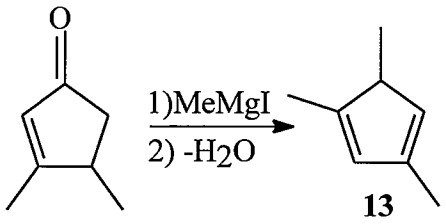


Collins et al., have reported the synthesis of **12**.[7] By treating **6**, with 2 equivalents of $MeLa(OTF)_2$ followed by the addition of PCC (pyridinium chlorochromate), pyridine and CH_2Cl_2 gave **11**, in 90% yield. Treatment of **11**, with 2 equivalents of $MeLa(OTF)_2$ followed by dehydration gave **12** in 40% yield.



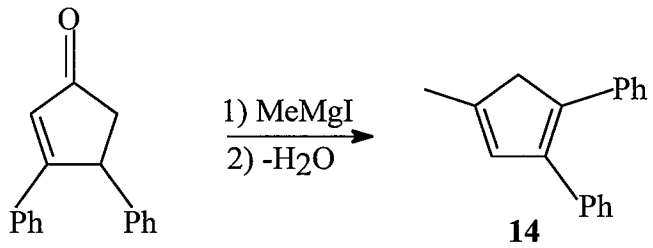
6 11 12

Davis et al., have reported the synthesis of 1,3,5-trimethylcyclopentadiene, **13**, by the addition of methyl magnesium iodide to 3,4-dimethylcyclopent-2-enone followed by spontaneous dehydration.[9] No yield was given.



13

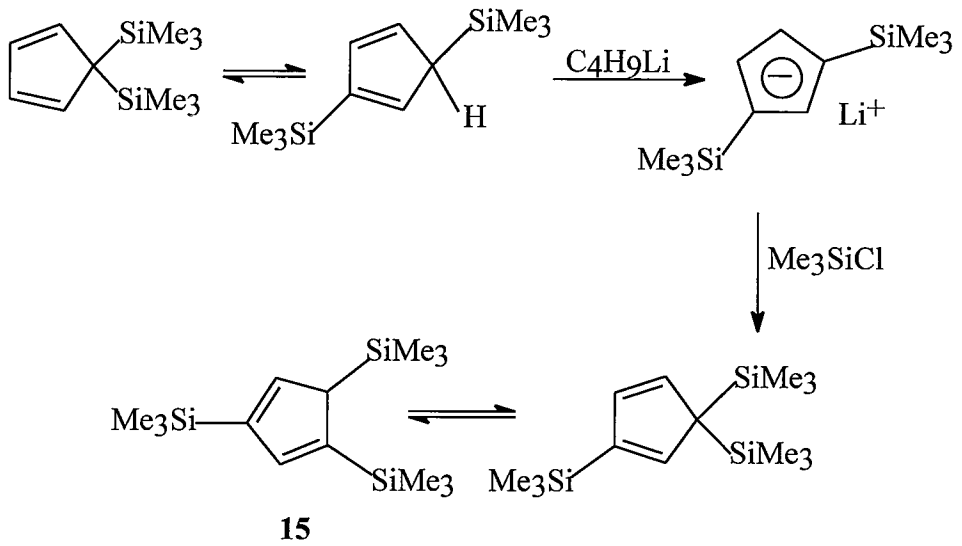
Rio and Charift have prepared 4-methyl-1,2-diphenylcyclopentadiene, **14**, in 60% yield, using a procedure similar to that used by Davis et al.[10]



14

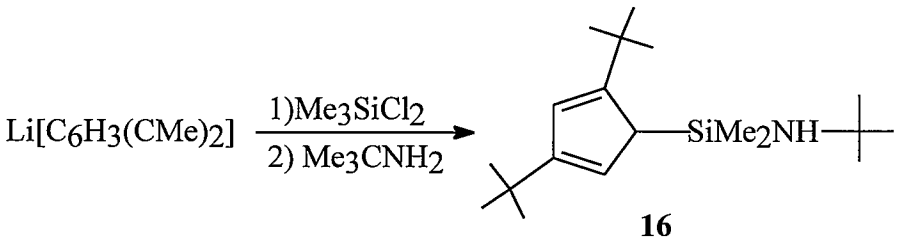
The addition of methyl magnesium iodide to 3,4-diphenylcyclopent-2-enone followed by subsequent dehydration gave **14**.[10]

Jutzi and Sauer reported the synthesis of **15**.[11] The addition of n-butyl lithium to bis(trimethylsilyl)cyclopentadiene followed by treatment with trimethylsilyl chloride gave **15** in quantitative yield.[11]



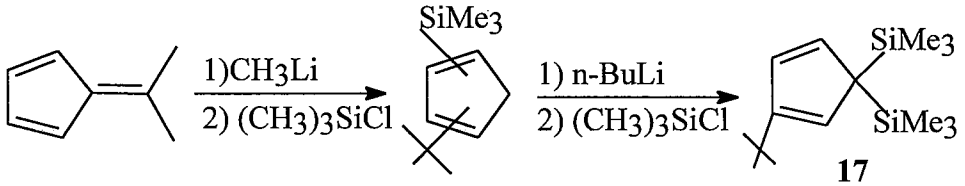
15

Okuda has reported the synthesis of **16**, by the addition of dichlorodimethylsilane to lithium di-*t*-butylcyclopentadienide, followed by the addition of *t*-butylamine.[12]



16

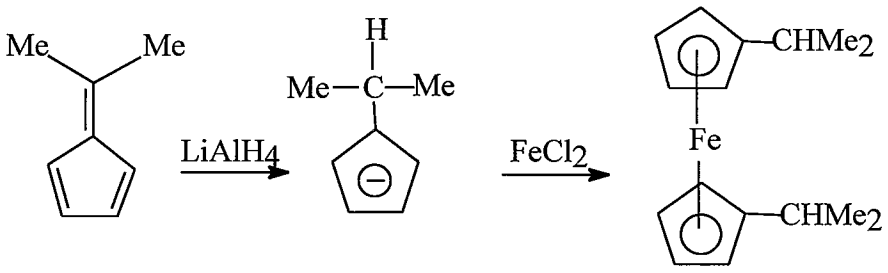
Okuda has also reported the synthesis of **17**, by the addition of CH_3Li to 6,6-dimethylfulvene, followed by the addition of $(CH_3)_3SiCl$ and the subsequent addition of n-BuLi and chlorotrimethylsilane.[13]



17

Highly Substituted Cyclopentadienyl Iron Complexes

Knox and Pauson have reported the synthesis of di-isopropyl ferrocene, **18**, by the addition of lithium aluminum hydride to dimethylfulvene followed by the addition of ferrous chloride in tetrahydrofuran.[14]



18

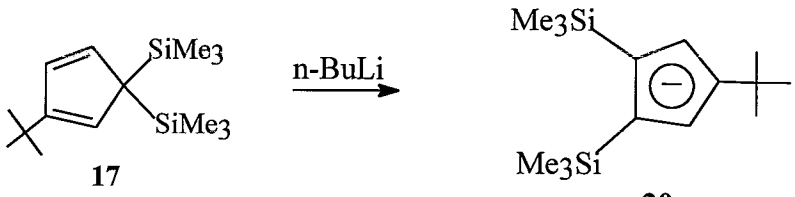
Little and Koestler prepared **18** in a similar manner. Inverse addition of ferrous chloride tetrahydrofuranate to the adduct of dimethylfulvene and lithium aluminum hydride produced **18** in 39% yield.[15]

Bunel et al., have reported the reaction of lithium salts of 1-(*p*-bromophenyl)-3,4-dimethylcyclopentadiene, **9**, with ($\eta^5C_5Me_3$)Fe(acac) to give **19** in 58% yield (acac = acetylacetonate).[8]

$$(C_5Me_5)Fe(CO)(acac) \xrightarrow[THF,\ -Li(acac)]{Li[C_5Me_5\text{-}p\text{-}C_6H_4Br]} (C_5Me_5)Fe(C_5Me_5\text{-}p\text{-}C_6H_4Br)$$

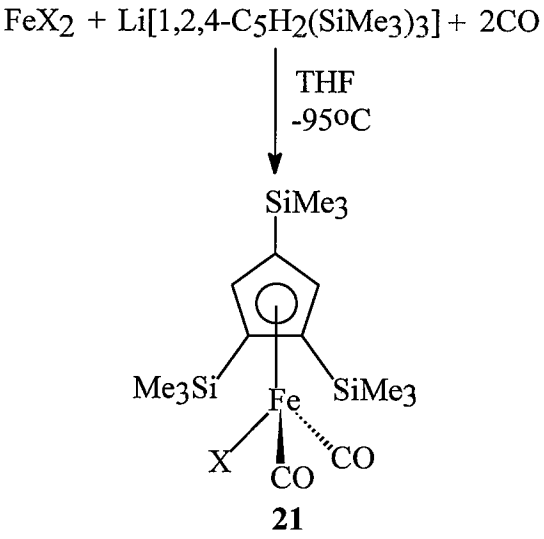
19

Okuda has reported the preparation of compound, **20**, by adding n-BuLi to 2-*t*-butyl-5,5-bis(trimethylsilyl)cyclopentadiene, **17**.[13]



17 20

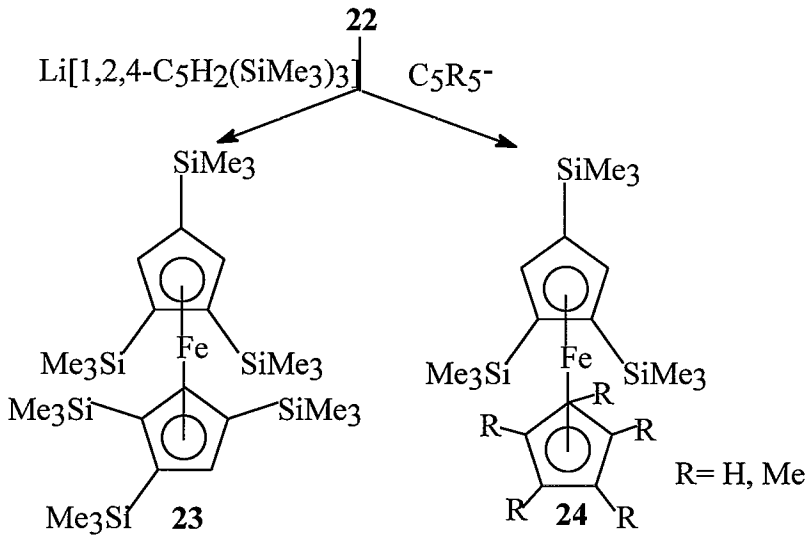
Okuda has reported the synthesis of **21**.[16] The reaction of ferrous halides FeX_2 (X=Cl, Br, I) with Li[1,2,4-$C_5H_2(SiMe_3)_3$] in THF at approximately -95 °C followed by the trapping of CO gave the complexes [η^5–1,2,4-$C_5H_2(SiMe_3)_3$]$Fe(CO)_2X$, **21** (X=Cl, 53% yield, X=Br, 65% yield, X=I, 58% yield).[16]



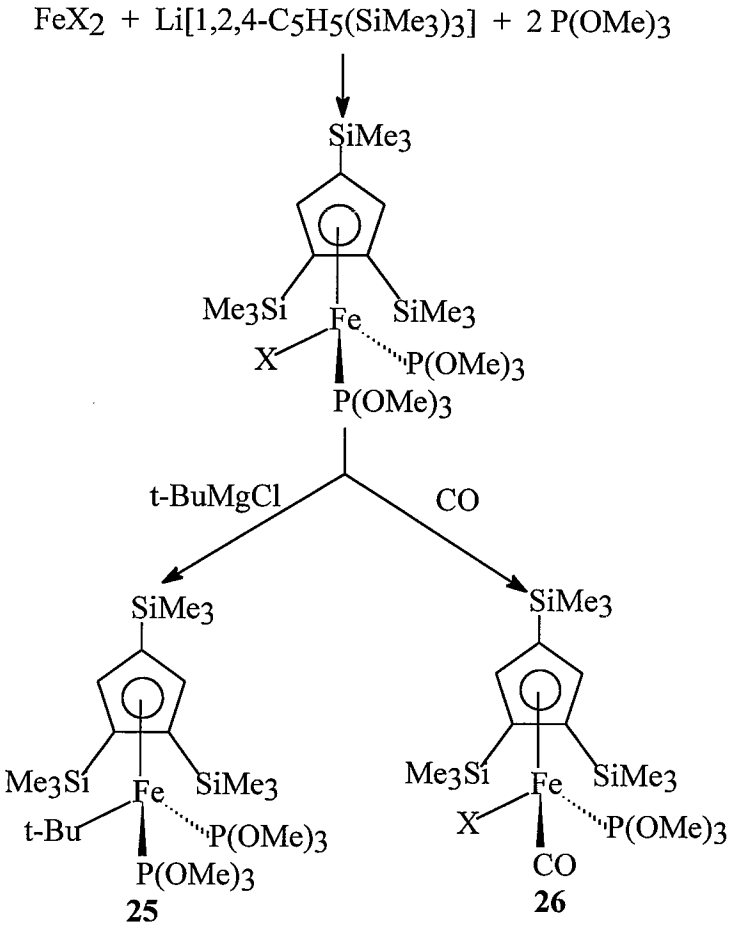
21

Okuda has also prepared compound **22**. The addition of $FeCl_2$ to Li[1,2,4-$C_5H_2(SiMe_3)_3$] at -40°C gave {Fe[1,2,4-$C_5H_2(SiMe_3)_3$]Cl}, **22**. Treatment of **22** with Li[1,2,4-$C_5H_2(SiMe_3)_3$] gave 1,1',2,2',4,4'-hexakis-(trimethylsilyl)iron, Fe[η^5–1,2,4-$C_5H_2(SiMe_3)_3$]$_2$, **23**. Treatment of **22** with $C_5R_5^-$ where R = H or Me gave **24**.[17]

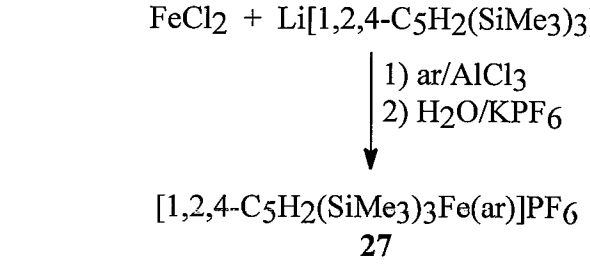
$FeCl_2$ + Li[1,2,4-$C_5H_2(SiMe_3)_3$] ⟶ Fe[1,2,4-$C_5H_2(SiMe_3)_3$]Cl
22

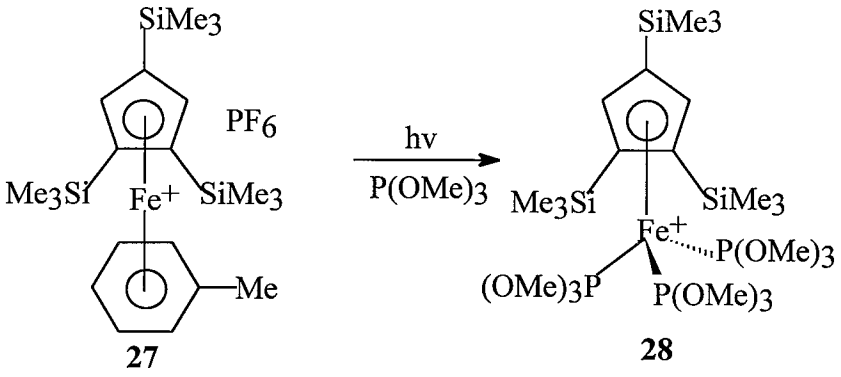


The reaction of FeX_2 with Li[1,2,4-$C_5H_2(SiMe_3)_3$] followed by two equivalents of $P(OMe)_3$, and the addition of *t*-BuMgCl gave **25**.[18] The addition of FeX_2 and 2 equivalents of $P(OMe)_3$ to Li[1,2,4-$C_5H_2(SiMe_3)_3$], followed by the addition of CO gave **26**.

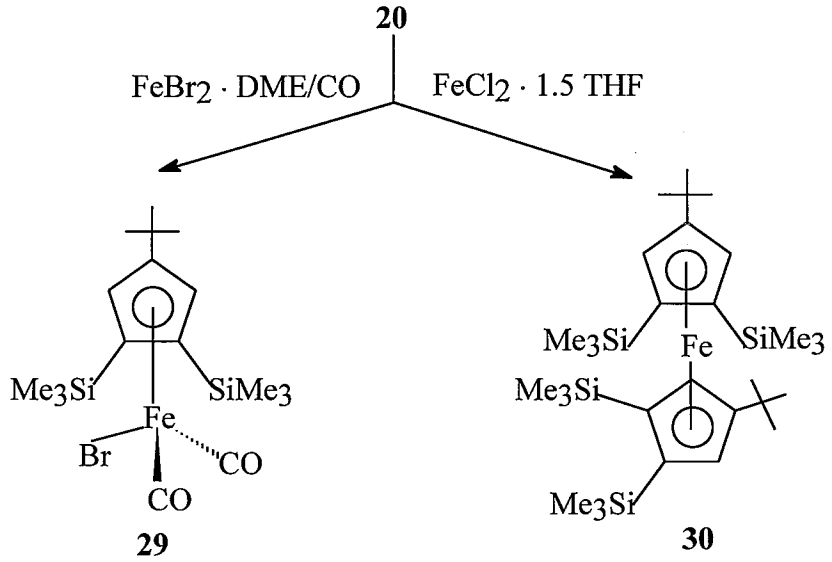


Addition of $FeCl_2$ to $Li[1,2,4\text{-}C_5H_2(SiMe_3)_3]$ followed by the addition of $ar/AlCl_3$, then H_2O and KPF_6 gave **27** (ar = C_6H_5, C_6H_5Me, $1,3,5\text{-}C_6H_3Me_3$).[17] When ar = C_6H_5Me, treatment of **27** with $P(OMe)_3$ under photolysis gave compound **28**.





Treatment of **20** with ferrous bromide in DME with carbon monoxide gave compound **29**. Treatment of **20** with $FeCl_2 \cdot 1.5$ THF gave compound **30**.[13]



CHAPTER 2

EXPERIMENTAL

General Laboratory Materials and Equipment

Operations were performed under an inert atmosphere on a double manifold schlenk line or in a Vacuum Atmosphere glovebox under an atmosphere of dry nitrogen. Ether, THF and hexanes were purified by distillation from Na/K alloy under nitrogen. Crotonic acid (Aldrich), isopropanol (Fisher), p-toluenesulfonic acid (Aldrich), benzene (Fisher), sodium bicarbonate (Fisher), magnesium sulfate (Fisher), polyphosphoric acid (Aldrich), sodium chloride (Fisher), ethyl ether (Fisher), triphenylphosphine (Aldrich), bromodiphenyl methane (Aldrich), bromine (Aldrich), triethyl amine (Aldrich), methyl lithium (Aldrich), and ferrous chloride (Aldrich) were used as received.

^1H NMR spectra were recorded at 250 MHz on a Bruker WM 250 spectrometer. Spectra were measured at ambient temperature in $CDCl_3$ using trimethylsilane as an internal standard. IR spectra were taken on an Impact 400 by Nicolet and processed using the software Omnic. Spectra were measured using

chloroform as a background for solid samples. Melting points were recorded on a MEL-TEMP II by LABORATORY DEVICES and are uncorrected.

Isopropyl-2-butenoate was prepared by a method reported by Conia.[19] This method was modified using polyphosphoric acid instead of phosphoric acid and P_2O_5 by Liu.[20] The synthesis of 3,4-dimethylcyclopent-2-enone was attempted by a local modification of Conia's procedure. [20] $[(Ph)_3P\text{-}CH(Ph)_2]^+Br^-$ was prepared from literature methods.[19]

Attempted Preparation of Diphenylmethylene-2,3-dimethylcyclopent-2-ene

To a solution of n-BuLi 1.2 mL (1.9 mmol) and 20 mL of ether was added 0.96 g (1.9 mmol) of $[(Ph)_3P\text{-}CH(Ph)_2]^+Br^-$. The solution was allowed to stir for 4 h at room temperature. 3,4-dimethylcyclopent-2-enone (*see Results and Discussion*) was added dropwise to the solution. The mixture was heated under reflux overnight, allowed to cool to room temperature and the precipitate was collected by vacuum filtration. The precipitate was washed with 10 mL of ether and the ethereal filtrate was extracted with three 10-mL portions of water. The aqueous layer was then back extracted with three 10-mL portions of ether. The ether layers were combined and dried over $MgSO_4$. Solvent was removed under vacuum. ^1H NMR (250 MHz, $CDCl_3$); 7.70-7.25 (m, Ar); 2.17(s, 3H); 1.68 (s, 3H); 1.25 (s, 3H).

Attempted Preparation of Diphenylmethylene-2,3-dimethylcyclopent-2-ene

To a solution of 60 mL of THF and 9.7 g (18 mmol) of $[(Ph)_3P\text{-}CH(Ph)_2]^+Br^-$ was added 13.3 mL (18 mmol) of MeLi dropwise via an addition funnel to a 3-neck flask equipped with a nitrogen inlet adapter and a reflux condenser. The solution was stirred at room temperature for 4 h after which time 2.0 g (18 mmol) of 3,4-dimethylcyclopent-2-enone (*see Results and Discussion*) was added dropwise. The resulting solution was allowed to stir under reflux for 48 h. The resulting white precipitate was collected by suction filtration. The precipitate is washed with two 10-mL portions of ether and the filtrate was washed with three 10-mL portions of distilled water. The water portions were back extracted with ether and the ether layers combined. The ether layer was dried over $MgSO_4$ and solvent removed under vacuum. The resulting orange, oily solution was washed with hexanes and the crystals (mp 128^o - 130^o) that were formed were collected by suction filtration and dried under vacuum. ^1H NMR (250 MHz, $CDCl_3$); 7.71-7.26 (m, Ar); 1.79 (s, 3H); 0.87 (s, 3H); 0.84 (d, 1H).

Elemental Analysis; Calculated for $C_{20}H_{20}$: C% 92.26; H% 7.74. Found: C% 77.49; H% 5.44.

Attempted Preparation of 3,4-Dimethyl-6,6-diphenylfulvene

Diphenylmethylene-2,3-dimethylcyclopent-2-ene (*see Results and Discussion*), 0.489 g (5.4 mmol), in ether was cooled to -78 C. Bromine, 0.15 mL

(5.4 mmol), was added dropwise at -78 C and the solution was allowed to stir for 30 minutes. The solution was allowed to warm to room temperature and Et_3N was added. The resulting solution was allowed to stir for 5 h at room temperature. The resulting precipitate was removed by vacuum filtration and the ether layer was washed with three 10-mL portions of water. The aqueous layer was back extracted with three 10-mL portions of ether and the ether layers combined. The ether layer was dried over $MgSO_4$ and the solvent removed under vacuum. ^1H NMR (250 MHz, $CDCl_3$); 7.72-7.37 (m, Ar); 2.09 (d, 1H); 1.61 (s, 3H); 1.22-1.19 (m, 6H).

Attempted Preparation of 3,4-Dimethyl-6,6-diphenylfulvene

To 50 mL of ether was added 1.404 g (5.4 mmol) of diphenylmethylene-2,3-dimethylcyclopent-2-ene (*see Results and Discussion*). The resulting solution was stirred and cooled to -40 C. 0.28 mL (5.4 mmol) of Br_2 was added dropwise and the resulting orange solution was stirred for 30 minutes and allowed to warm to room temperature. 1.50 mL (10.8 mmol) of triethylamine was added at room temperature and the solution was allowed to stir for 4 h. The precipitate was removed by suction filtration and the filtrate was washed with three 10-mL portions of 5% HCl then washed with three 10-mL portions of distilled water. The aqueous layers were back extracted with three 10-mL portions of ether. The solvent was removed leaving orange crystals (mp 134° - 136°). ^1H NMR (250 MHz, $CDCl_3$); 7.70-7.43 (m, Ar); 2.16 (s, 3H).

Elemental Anaylsis; Calculated for $C_{20}H_{18}$: C% 92.98; H% 7.02. Found: C% 68.54; H% 5.15

Attempted Preparation of 1,1'(bis[1,1-Diphenylethyl)-3,3',4,4'-tetramethylcyclopentadienyl]iron

Methyllithium, 5.0 mL of 1.5 M in diethyl ether (7.5 mmol) was added dropwise to 1.935 g (7.5 mmol) of 3,4-dimethyl-6,6-diphenylfulvene (*see Results and Discussion*) in 30 ml of diethyl ether at 0 C, in a 100 mL three-necked round bottom flask equipped with a condenser, nitrogen inlet adapter and a septum capped pressure-equalizing dropping funnel. The resulting reaction mixture was stirred for 1 h at room temperature, then refluxed for 3 h during which time a white precipitate formed. The reaction mixture was cooled to 0° C and $FeCl_2$, 0.475 g (3.75 mmol), was added. The resulting solution was allowed to warm to room temperature and refluxed for 6 h. The reaction mixture was allowed to cool to room temperature and the solvent removed under vacuum to give a deep brown solid. This residue was taken up in 50 ml of benzene. The resulting suspension was then filtered and the solvent removed under vacuum to give 0.15 g of a bright yellow oil. ^1H NMR (250 Mhz, $CDCl_3$); 7.71-7.46 (m, Ar); 2.17 (s, 3H); 1.65 (s, 3H).

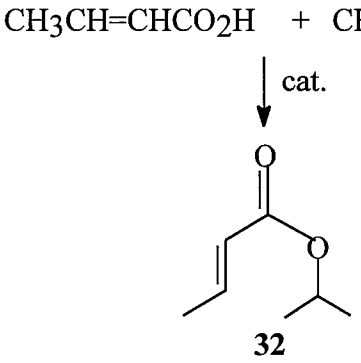
Elemental Analysis; Calculated for $C_{42}H_{44}Fe$:C% 83.74; H% 6.99. Found: C% 36.05; H% 8.24.

CHAPTER 3

RESULTS AND DISCUSSION

The goal of the research presented was to develop a high yielding method for the preparation of a tetrasubstituted fulvene and to prepare a ferrocene complex incorporating a new tetrasubstituted cyclopentadienyl ligand prepared from the fulvene.

Isopropyl-2-butenoate, **32**, was prepared in 89% yield by the addition of crotonic acid, 2-propanol and p-toluenesulfonic acid to benzene.[18]



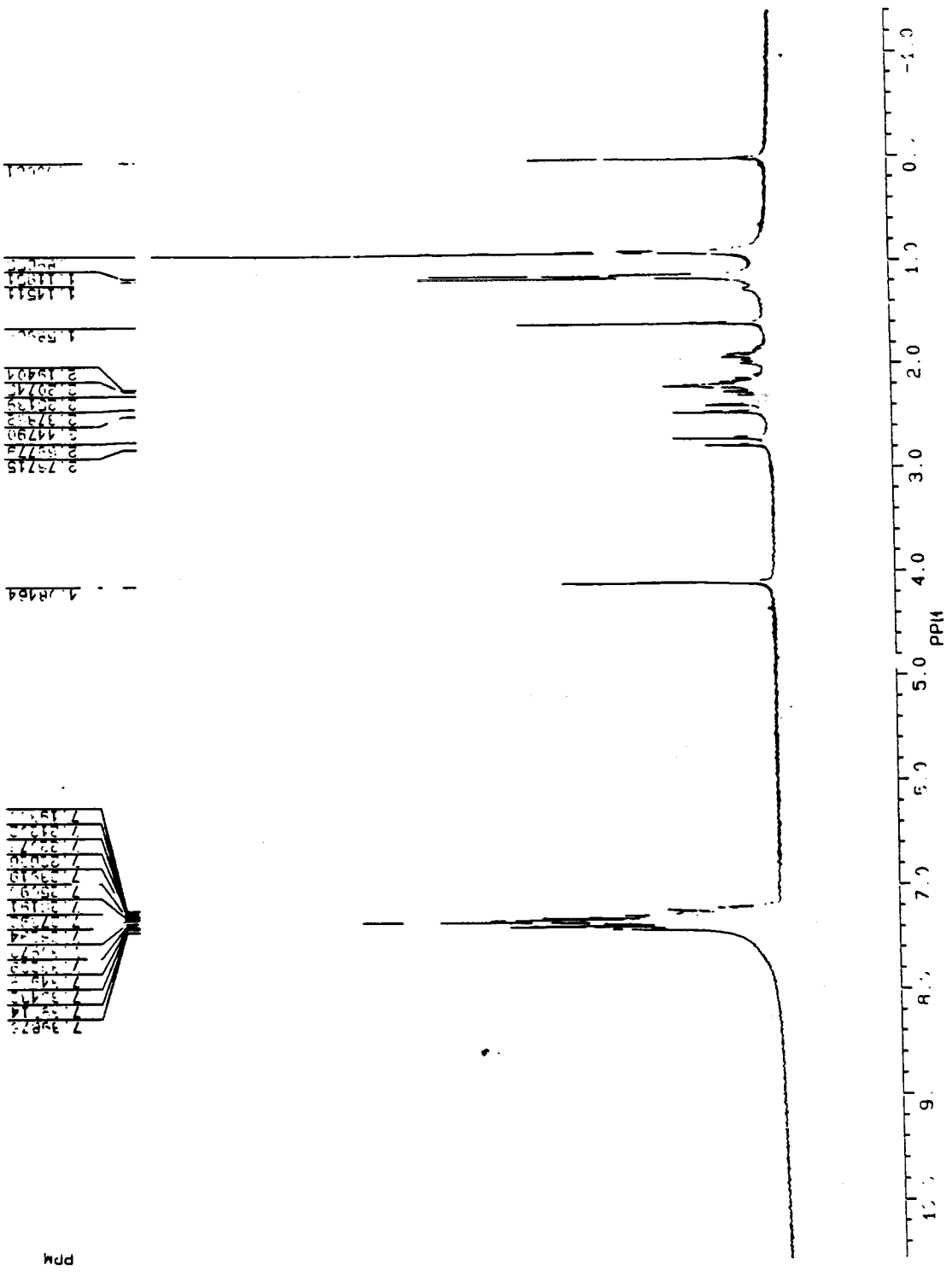
32

The treatment of **32** with polyphosphoric acid did not result in the synthesis of dimethylcyclopent-2-enone, **33**. The published procedure for 3,4-dimethylcyclopent-2-enone was incorrect. Several synthesis modifications were

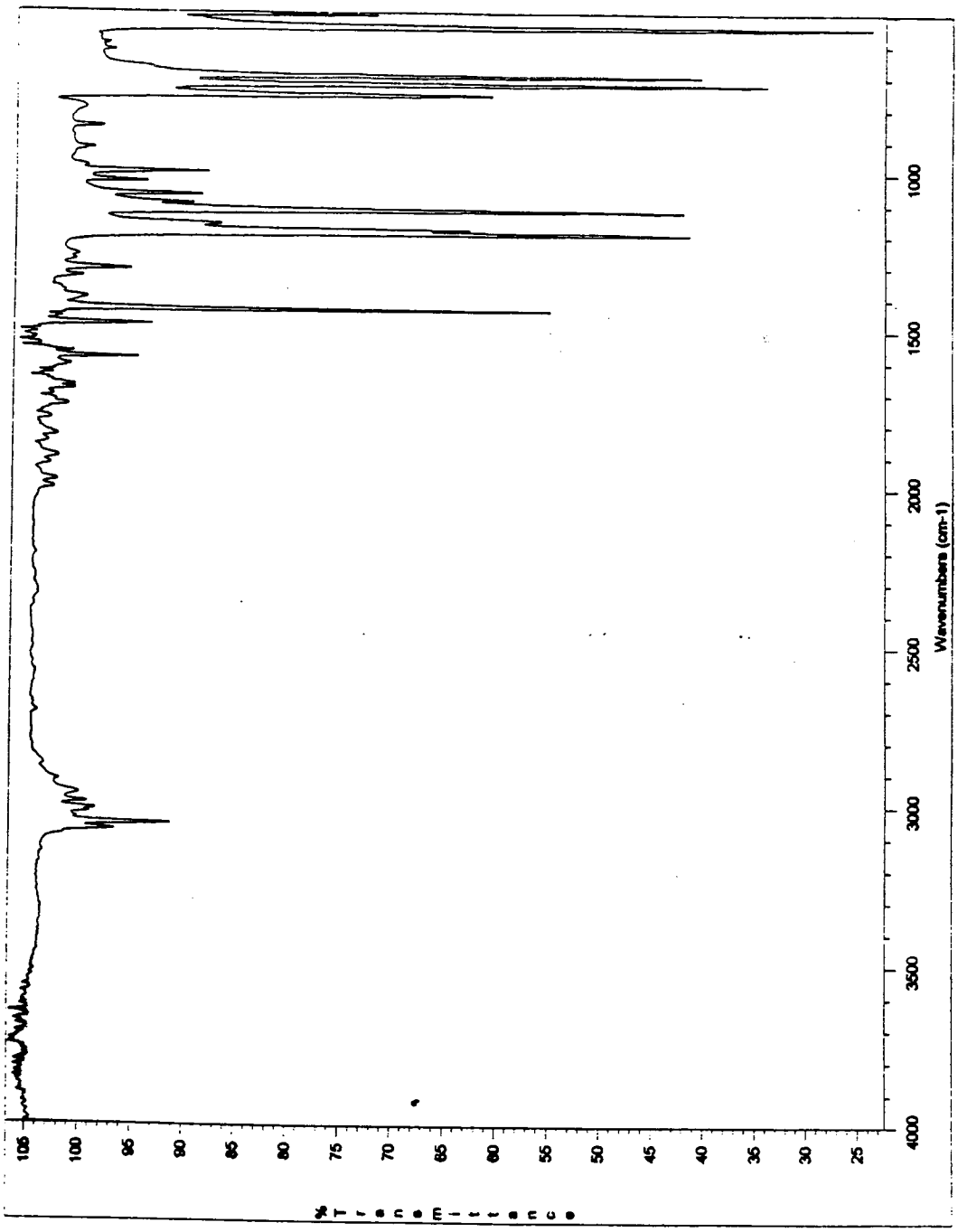
attempted and all were unsuccessful. Careful NMR, elemental analysis and infrared spectroscopy conclude that none of the syntheses was successful. Earlier it was incorrectly concluded that **33** was successfully synthesized and therefore was used to carry out the synthesis of **35**, which was used to carry out further synthesis of other compounds.

APPENDIX 1

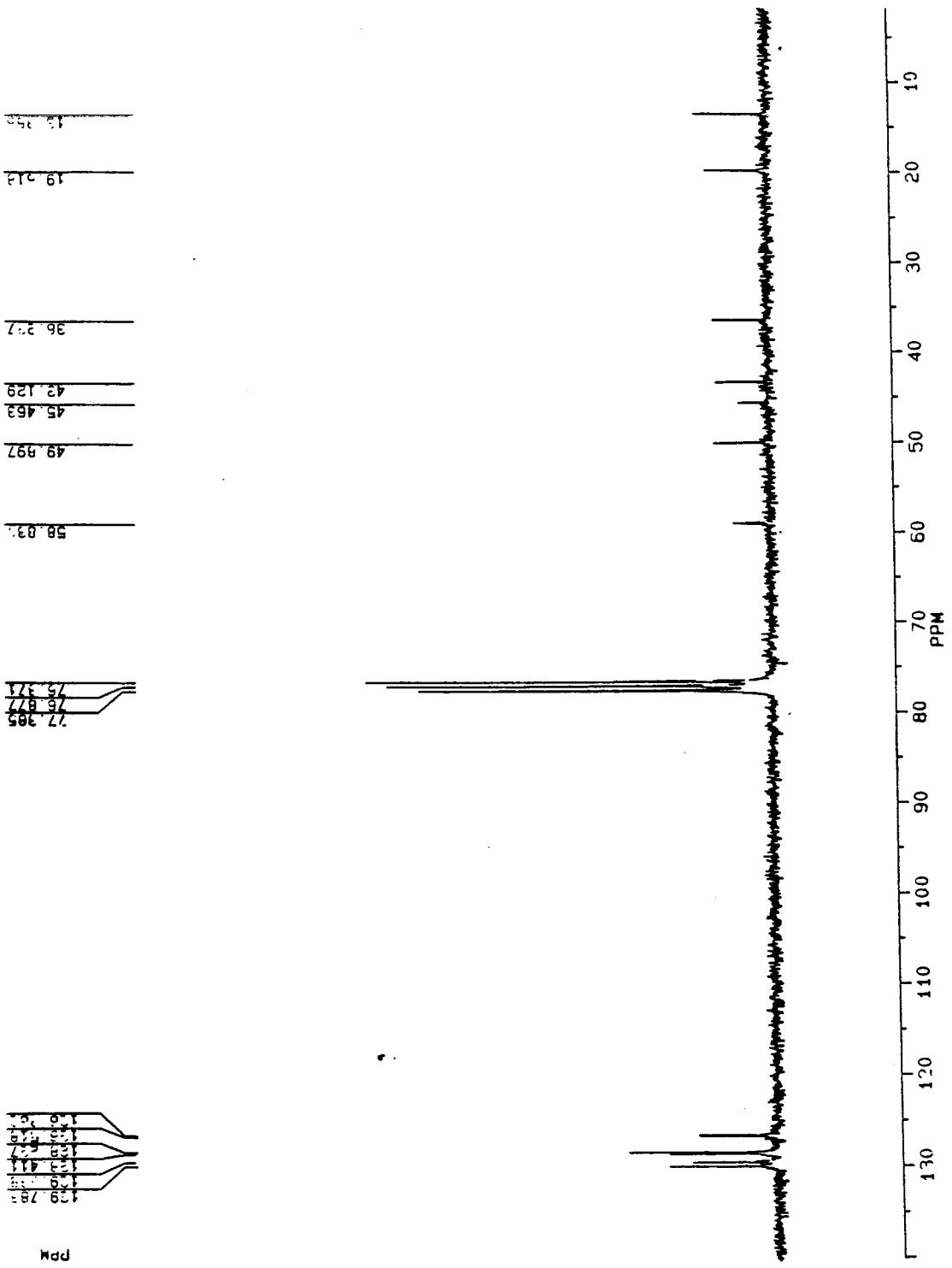
SPECTRA OF COMPOUND 35



Proton NMR Spectrum of Compound 35



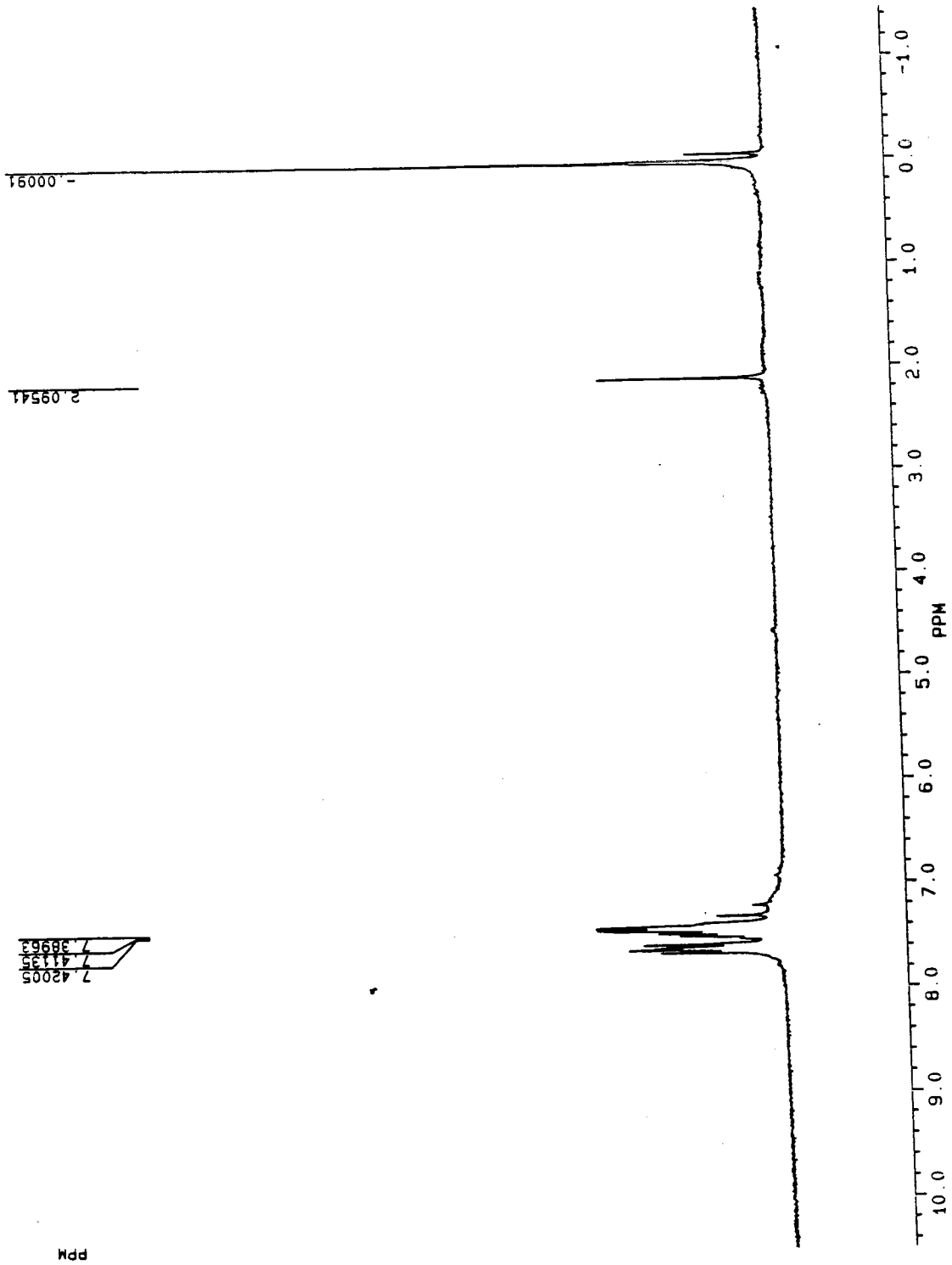
Infrared Spectrum of Compound 35



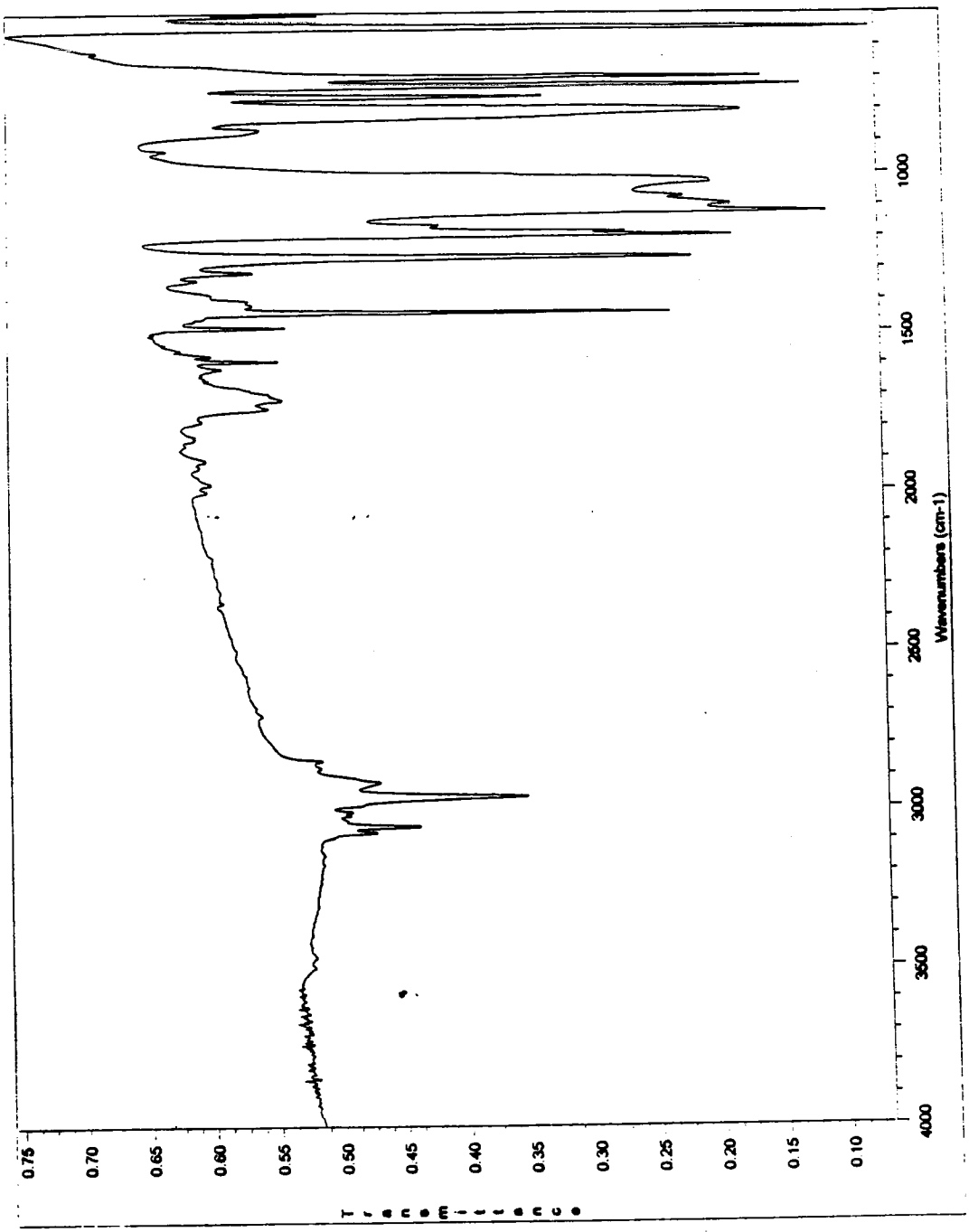
Carbon-13 NMR Spectrum of Compound 3

APPENDIX 2

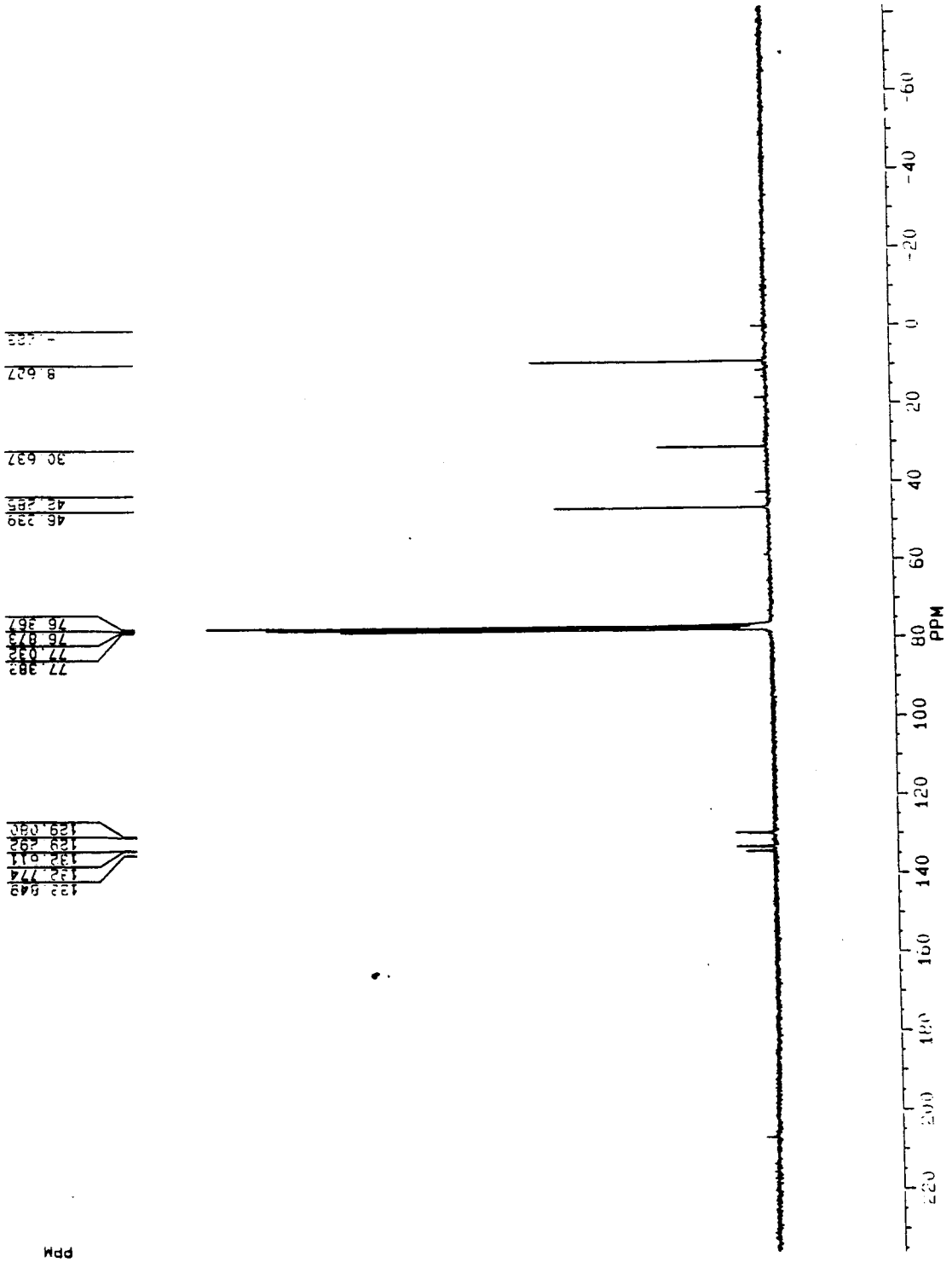
SPECTRA OF COMPOUND 36



Proton NMR Spectrum of Compound 36



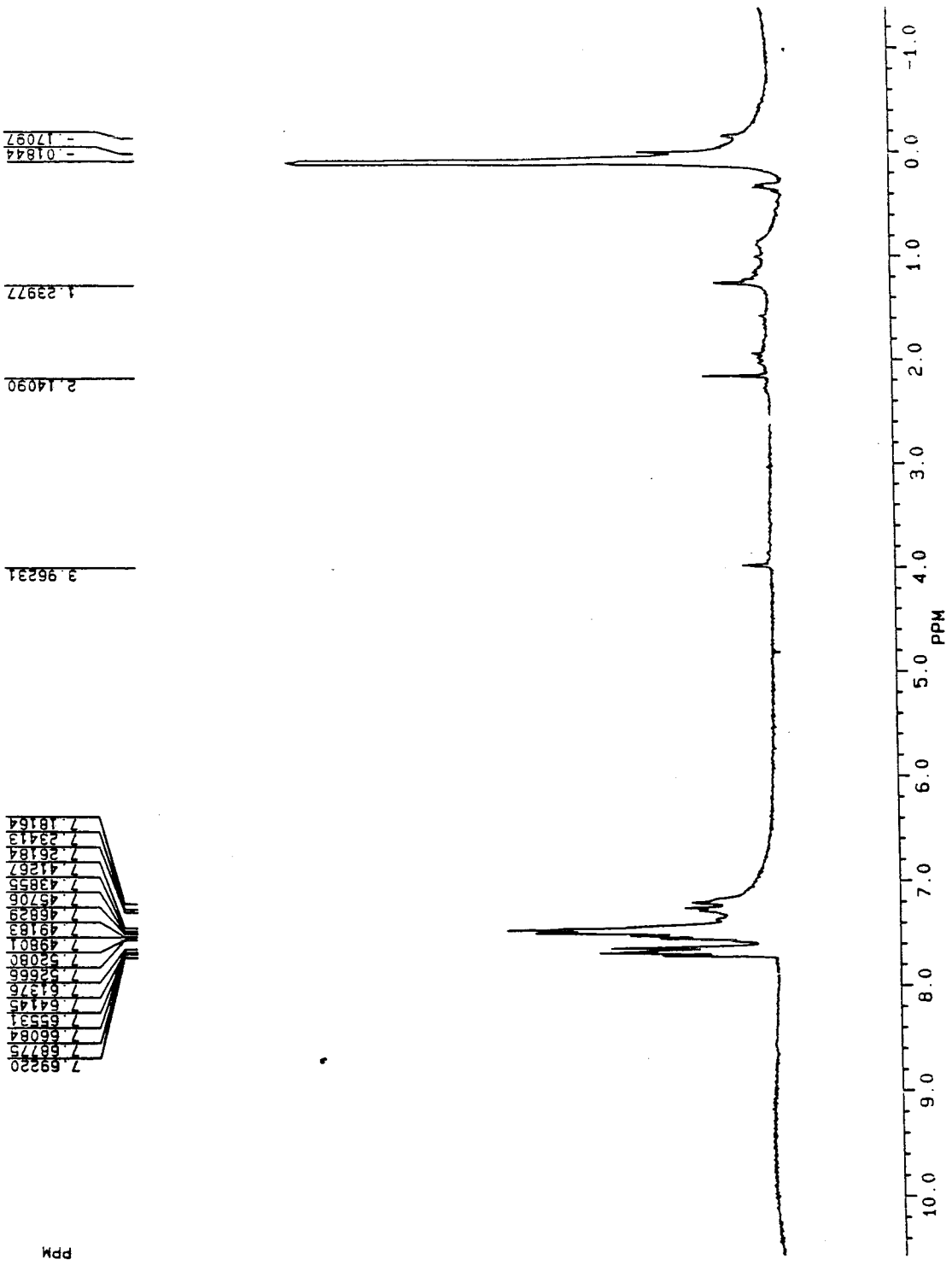
Infrared Spectrum of Compound 36



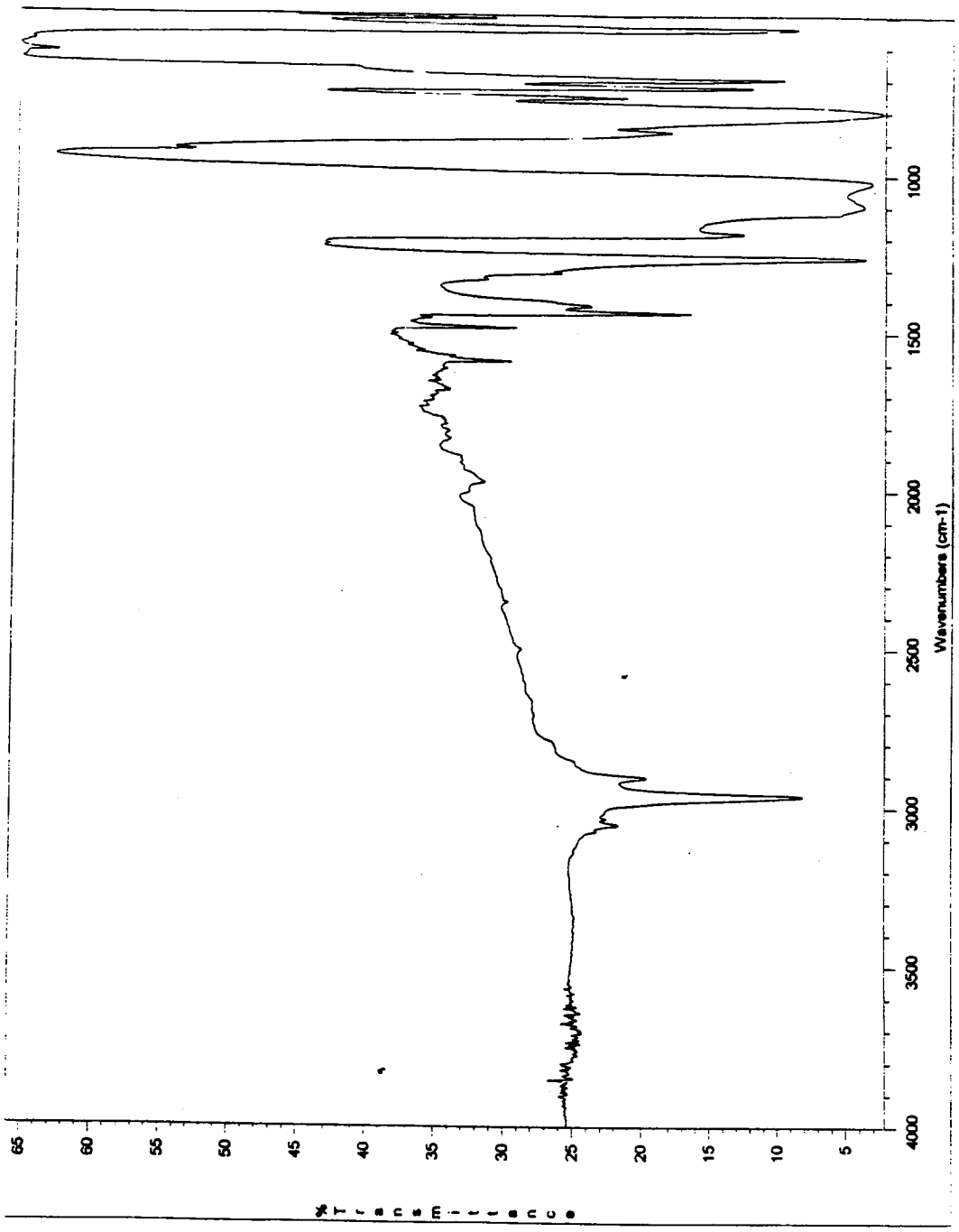
Carbon-13 NMR Spectrum of Compound 36

APPENDIX 3

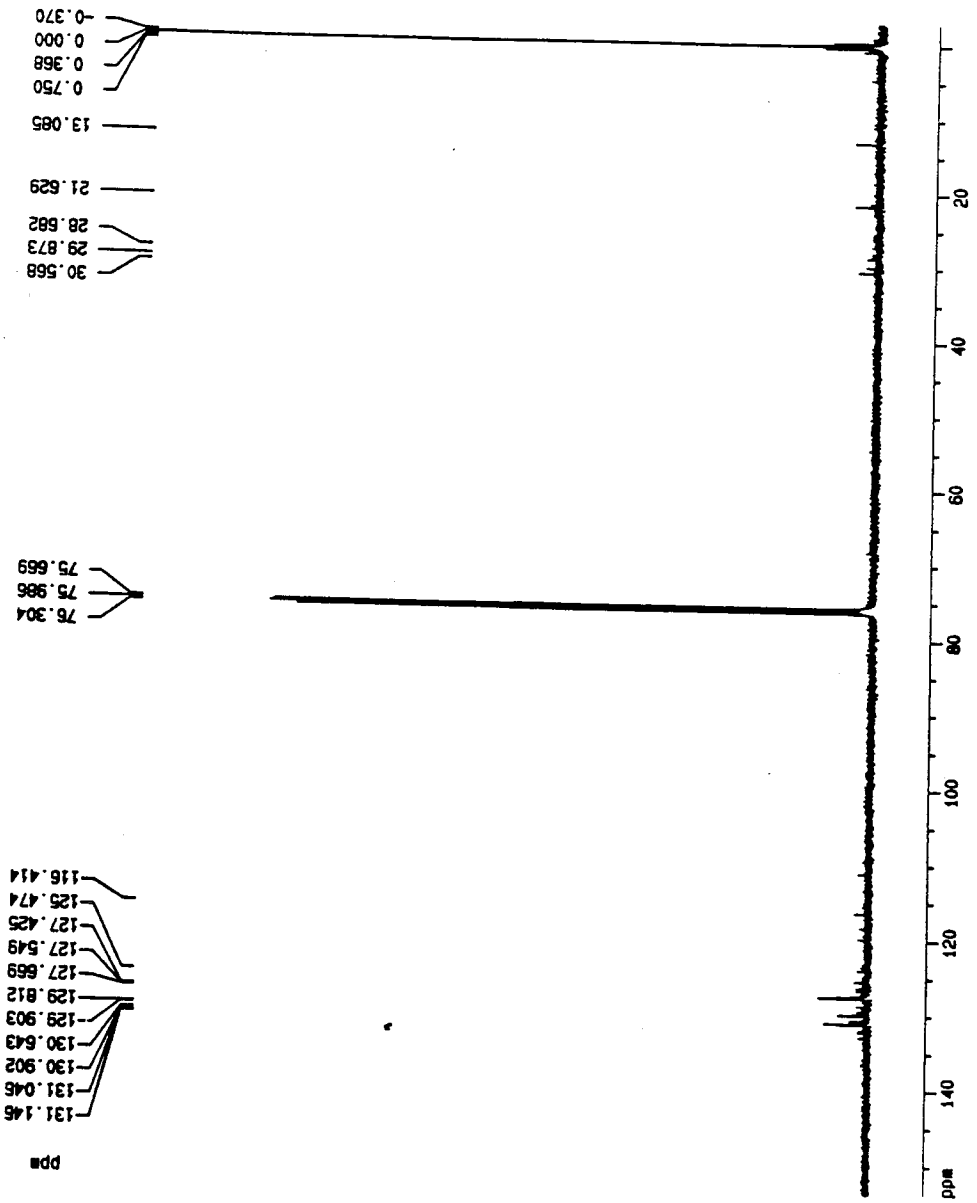
SPECTRA OF COMPOUND 37



Proton NMR Spectrum of Compound 37



Infrared Spectrum of Compound 37



Carbon-13 NMR Spectrum of Compound 37

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